THE DYNAMICS OF CYTOKINES LEVEL AND MYOCARDIAL ISCHEMIA INDICATORS IN PATIENTS WITH CORONARY HEART DISEASE WHEN EXPOSED TO QUERCETIN

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Introduction. For many years, coronary heart disease (CHD) has been the leading cause of mortality in the world. Coronary atherosclerosis (AS) is the morphological basis of CHD. In the formation of atherosclerotic plaque, the leading role of numerous inflammatory mediators and reactions involving immunocompetent cells has been proven [1].

Today, myocardial changes in CHD are represented as an ischemic-reperfusion injury, which is a complex process involving the interaction of a number of cells, including endothelium and immunocompetent cells, as well as the coagulation system components. The activation of chronic systemic inflammation (CSI) underlies endothelial dysfunction, vasoconstriction, platelet activation, and myocardial microcirculation impairment. Proinflammatory cytokines (CK) promote the expression of pain mediators, activate the vagus afferent receptors, and cause a negative inotropic effect [2].

The molecular mechanisms of atherogenesis and myocardial impairment in CHD are studied in detail in order to find new targets for pharmacological effect. According to modern scientific research, polyphenolic compounds of natural origin possess numerous mechanisms of anti-inflammatory activity, implemented at different levels of cellular organization [3, 4].

The aim of our research was to study the indicators of chronic systemic inflammation in patients with stable coronary heart disease, their relationship with the parameters of myocardial ischemia and the effect of quercetin on the detected disorders.

Materials and methods. The study included 85 patients of both sexes, aged from 48 to 67, with the diagnosis of coronary heart disease: stable exertional angina, FC II, HF 0-I. Patients were divided by random sampling into 2 groups – the study group (30 patients) and the comparison group (55 patients). Patients were examined to determine the level of tumor necrosis factor alpha (TNFα) and interleukin-1β (IL-1β) in the serum by immunoenzymatic assay, the content of fibrinogen (FG) in the blood plasma by weight and 24-hour ECG Holter monitoring (HM) was performed with the calculation of total myocardial ischemia – the total duration of episodes of ST segment depression (Σt ST depr) and the total number of episodes of ST depr in three registration leads [5, 6]. All patients received standard therapy (β-blockers, statins, aspirin), patients in the study group were additionally prescribed quercetin at a dose of 120 mg per day. In 2 months, patients were re-examined to the aforementioned extent of studies.

Results. All patients with coronary heart disease had an elevated blood level of TNFα (8.68±2.44 pg / ml) and IL-1β (9.58±3.24 pg / ml), FG content in the blood plasma was elevated in 37% of patients. The daily Σt ST depr was

52.92±13.00 min. The number of episodes of ST depr was 10.58±2.83. We found a direct correlation relationship of moderate strength between the level of TNFα and Σt ST depr ($r=0.3363$, $p<0.01$), TNFα level and the number of episodes of ST depr ($r=0.413$, $p<0.01$), the content of FG and Σt ST depr ($r=0.408$, $p<0.01$), and the content of FG and the number of episodes of ST depr ($r=0.410$, $p<0.001$). These findings demonstrate the correlation between chronic systemic inflammation and myocardial ischemia. After two months of treatment in the comparison group, there were no reliable changes in the levels of proinflammatory cytokines. The exposure to quercetin significantly decreased the level of IL-1β (by 17.4%, $p=0.002$) and TNFα (by 23%, $p=0.048$). In both groups, the level of fibrinogen was reliably decreased, but more significantly under the influence of quercetin ($p=0.0004$). According to the data of ECG HM, in the study group, the number of episodes of ST depr decreased by 27.6%, whereas in the comparison group – by 15.9%. In patients of the comparison group, Σt ST depr decreased by 20.7%, in patients who additionally received quercetin – by 34.9% (up to 32.7±13.08 min.), and the value was significantly different from that of the comparison group ($p<0.05$).

Conclusion. In patients with CHD, the increased level of chronic systemic inflammation correlates with the severity of myocardial ischemia. The use of quercetin in the comprehensive therapy of patients with CHD had an anti-inflammatory effect, and contributed to a decrease in the number and duration of episodes of myocardial ischemia, which may be due to its anti-inflammatory properties.

Prospects for further research. The obtained results substantiate the expediency of using the inflammatory markers for assessing the course and progression of CHD. The detected efficacy of quercetin in the correction of CSI level and myocardial ischemia forms the basis for further research to include it in the integrated therapy of CHD.

The results of the study demonstrate the need for further in-depth study of the molecular mechanisms of CHD pathogenesis for the development of new therapeutic strategies to improve patients' quality of life.

Key words: coronary heart disease, chronic systemic inflammation, myocardial ischemia, quercetin.

References:

1. Montalescot, G., Sechtem, U., Achenbach, S., Andreotti, F., Arden, C., Budaj, A., et al., 2013. 2013 ESC guidelines on the management of stable coronary artery disease. Eur Heart J. 34, pp. 2949–3003.
2. Sharma, H.S. & Das, D.K., 1997. Role of cytokines in myocardial ischemia and reperfusion. Mediators Inflamm. 6(5), pp. 175-183.
3. Andriantsitohaina, R., Auger, C. & Chataigneau, T., 2012. Molecular mechanisms of the cardiovascular protective effects of polyphenols. Br. J Nutr. 108(9), pp.1532-1549.
4. Jin, H.B., Yang., Y.B., Song Y.L., Zhang, Y.C. & Li, Y.R., 2012. Protective roles of quercetin in acute myocardial ischemia and reperfusion injury in rats. Mol. Biol. Rep. 39, pp. 11005-11009.

5. Chekalina, N.I., Shut`, S.V., Trybrat, T.A., Burmak, Yu.H., Petrov, Ye.Ye., Manusha, Yu.I. & Kazakov, Yu. M., 2017. Effect of quercetin on parameters of central hemodynamics and myocardial ischemia in patients with stable coronary heart disease. Wiadomosci Lekarskie. (LXX)4. pp. 707-711.
6. Hashizume, M. & Mihara M., 2012. Atherogenic effects of TNF-α and IL-6 via up-regulation of scavenger receptors. Cytokine. 58(3), pp. 424–430.
7. Zharinov, O.J. & Kuc', V.O., 2010. Holterovskoe i fragmentarnoe monitorirovanie ECG. Kiïv : Medicina svitu; 2010, 128 p.